The Effects of Magnesium Sulfate Prophylaxis on Arrhythmia and Cardiac Performance in Coronary Artery Bypass Grafting

KORONER ARTER BYPASS CERRAHİSİNDE MAGNEZYUM SÜLFAT PROFİLAKSİSİNİN KARDİYAK PERFORMANS VE ARİTMİ ÜZERİNE ETKİLERİ

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Summary

The aim of this study was to evaluate the effects of magnesium sulfate on cardiac arrhythmia and performance in patients undergone coronaiy artery bypass grafting.

One hundred patients randomized into placebo (n=50) and magnesium (n=50) groups. The magnesium group received 1.5 g (12.16 mEq) magnesium sulfate intravenously during postoperative first 24 hours, delivered at every 4 hour intervals. The placebo group did not receive magnesium sulfate and served as control.

The magnesium group had significantly higher magnesium levels than the placebo group along the course of study (2.037±0.49 versus 1.738±0.41 mEq/L as mean, p = 0.001). Although there was not any significant difference regarding monitorized hemodynamic performances, the magnesium group had reduced levels of myocardial isoenzyme of creatine kinase (CK-MB) as an indicator of myocardial damage, at postoperative 12th hour and on postoperative day 1 (34.02±12.07 versus 45.98±25.80; p = 0.02 and 32.34±15.26 versus 44.58±41.25 IU/L; p = 0.043, respectively). The supraventricular arrhythmia incidence of magnesium group had lower than that of placebo group (2% versus 26%; p<0.002, as maximum incidence at postoperative 2th hour). No significant difference was demonstrated regarding ventricular arrhythmias, despite higher frequency in control group. Patients in magnesium group need less antiarrhythmic treatment, especially at perioperative and postoperative 12 hour periods (4% versus 16%>; p = 0.045 at both observation periods).

The results of our study suggest that magnesium prophylaxis prevents hypomagnesemia and reduces the incidence of supraventricular and somewhat ventricular tachyarrhythmias by enhancing myocardial protection.

Key **Words:** Magnesium, Arrhythmia, Cardiac Surgery

T Klin J Med Res 1999, 17:115-124

Received: May 22, 1999

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Özet

Çalışmamızın amacı koroner arter bypass cerrahisi geçiren hastalarda profilaktik magnezyum sülfat uygulamasının kardiyak aritmi ve performans üzerine etkilerini araştırmak idi.

100 hasta eşit olarak plasebo (n—50) ve magnesium (n=50) gruplarına rastgele ayrıldı. Magnesium grubuna 1.5 g (12.16 mEq) magnesium sülfat intravenöz olarak postoperatif ilk 24 saat süresince 4 saatlik peryotlarda verildi.

Çalışma süresince magnezyum grubunun magnezyum düzeyleri plasebo grubundan anlamlı olarak yüksekti (ortalama olarak 2.037±0.49 karşı 1.738±0.41 mEq/L, p = 0.001). Monitörize hemodinamik performanslar açısından anlamlı bir fark olmasa da magnesium grubunun miyokardiyal kreatin kinaz izoenzim düzeyi, miyokardiyal hasarın bir göstergesi olarak, postoperatif 12. saat ve 1. günde anlamlı derecede düşük bulundu (sırasıyla 34.02±12.07 karşı 45.98±25.80; p = 0.02 ve 32.34±15.26 karşı 44.58±41.25 IU/L; p = 0.043). Magnezyum grubundaki supraventriküler aritmi insidansı plasebo grubundan anlamlı olarak azdı (%2'ye karşı %26; p<0.002, postoperatif 2. saatteki maksimum değerler olarak). Kontrol grubunda daha sık görülmesine rağmen ventriküler aritmi açısından anlamlı fark yoktu. Özellikle perioperatif ve postoperatif 12. saat gözlemlerinde magnezyum grubunun antiaritmik ihtiyacı anlamlı derecede az oldu (%4'e karşı %16; p=0.045).

Çalışmamızın sonuçları magnezyum profilaksisinin hipomagnezemiyi önlediğini ve özellikle supraventriküler bir ölçüde de ventriküler aritmi insidansını miyokard koruyucu etkileri ile ilişkili olarak azalttığını göstermektedir.

Anahtar Kelimeler: Magnesium, Aritmi, Kardiyak Cerrahi

TKlin Araştırma 1999, 17:115-124

Magnesium (Mg^{2+}) is the second most important cation of intracellular compartment and acts as a cofactor in processes regulating transmembrane electrolyte gradients, energy metabolism, the synthesis of secondary messengers like adenylate cy-

clase, ion channels, and secretion of some hormones like parathormone (1). Magnesium has some well known circulatory effects, such as decrease in systemic vascular resistance, dilatation of coronary arteries, increase in cardiac output, decrease in platelet aggregation, protection against catecholamine derived myocardial necrosis and stabilisation of cell membrane (2). Moreover, 95% of intracellular adenosine triphosphate (ATP) is complexed with Mg^{2+} and this form is the enzymatically active one. Mg^{2+} affects all reactions running on ATP hydrolysis (3).

Total magnesium concentration decreases during cardiopulmonary bypass (CPB), because of corresponding increase in complexed forms with ultrafiltered fraction and hemodilution. Once the magnesium level has fallen below normal, it could be raised again very slowly, unless an active replacement was performed, due to lack of a hormonal control mechanism. (1, 2). There was an inverse relationship between blood Mg^{2+} level and mortality rate of ischemic coronary artery disease. It was asserted in invitro studies that magnesium insufficiency led coronary artery spasm, therefore it could cause the mortality (4, 5). Postoperative ventricular tachyarrhytmias (VTs) and supraventricular tachyarrhytmias (SVTs) occur in about 30% and 54% of patients respectively. Many drugs used for treatment or prophylaxis against these dysrhythmias are associated with significant untoward effects. Hypomagnesemia incidence can rise up to 70% in patients undergoing CPB (6, 7).

Mg^{2+} counteracts the effects of Ca^{2+} in exitation-contraction coupling, thereby reduces energy loss, as well as lead some electrophysiologic consequences such as, prolongation of sino-atrial conduction time, prolongation of atrioventricular node and refractory period and prolongation of P-R and A-H intervals. The antidysrhythmic properties of these effects are investigated thoroughly (8). Caspi and coworkers reported that magnesium prophylaxis in coronary artery bypass grafting had benificial effects on myocardial functions (9). Karmy-Jones and colleagues reported that magnesium prophylaxis reduced ventricular tachyarrhythmias (6). However, the efficacy spectrum of magnesium on dysrhytmias are still controversial.

This study was designed in a placebo controlled protocol in which the aim was to assess the effects of perioperative and postoperative administration of magnesium sulfate on arrhythmia and myocardial functions in patients with only coronary artery disease and undergoing coronary artery bypass grafting, providing to exclude any additional arrhythmogenic risk of other cardiac disturbances.

Materials and Methods

We studied one hundred patients undergoing elective coronary artery bypass grafting, after informed consent of each was obtained. The patients with preoperatively diagnosed renal failure, evidence of ongoing ischemia (angina and ST changes), taking antiarrhythmic therapy, undergoing reoperation or emergent operation were excluded. There were 50 patients in study as well as control groups. After randomization the magnesium group received 15 g=10 mL=12.16 mEq magnesium sulfate in 50 mL 5% dextrose solution intravenously, beginning at the termination of CPB and repeating at every 4 hours along the first postoperative 24 hours, thereby about 85 mEq Mg^{2+} was administered as sum of 7 dosages. The other 50 patients in control group had received only 50 mL 5% dextrose solutions, as placebo, at same intervals. Along the course of study, potassium (10 to 20 mEq potassium chloride in 50 ml normal saline solution) and calcium (1 g calcium gluconate in 50 mL normal saline solution) were administered to maintain the concentrations of potassium at least 3.5 mEq/L and calcium level at least 8.5 mEq/L. These interventions were directed to neglect the possible arrhythmogenic effects occurred with deficiency of these ions and to maintain acid-base balance.

There was not any significant difference between two groups regarding age, gender, ejection fraction (EF), cross clamping time, CPB time, number of grafting, concomittant diabetes, renal disease, chronic obstructive pulmonary disease (COPD), prior myocardial infarction (MI), prior arrhythmia and preoperative management of calcium blocker, (3 blocker, diuretic, digoksin incidences. The **P** blocker and Ca blocker therapies were continued until the day of operation, but digoksin was stopped at least two days before the operation.

Operative Technique

Anesthetic induction was performed with 5 mg/kg fentanyl, 3-5 mg/kg thiopental sodium, 1 mg/kg lidocain and 0.1 mg/kg pancuronium and enflurane was added as inhalatory anesthetic in management of anesthesia. A11 operations were performed through median sternotomy. CPB was established with single two stage venous cannula and an ascending aortic cannula. Moderately hypotermic blood cardioplegia containing 15 mEq magnesium sulfate and membrane oxygenator were preferred for both groups. During CPB hematocrit was maintained between 20% and 25%. The nonpulsatile pump flow was carried out at 2 to 2.5 L/min/m^2 and the mean arterial pressure was managed between 50 to 70 ímnHg during cross clamping. Only left internal mammarian artery and saphenous vein grafts were used.

Blood Magnesium Analyses

Plasma level of Mg^{2+} was measured from venous blood specimens drawn as preoperatively, under cross clamping, at postoperative 2, 6 and 12 hours and on postoperative days 1 and 2, by spectrophotometric analysis (Hitachi-704 autoanalyser). The measured values were total magnesium concentration.

Hemodynamic Measurements and Computations

A triple lumen-thermodilution catheter (Swan-Ganz) was inserted through internal jugular vein of each patient and positioned 3 to 4 cm distally to pulmonary valve. By using the Swan-Ganz catheter and computerised system (Horizon XL, Mennen Medical Inc, Clarence NY) hemodynamic data including arterial pressure (mmHg), heart rate, electrocardiography, right atrial pressure (CVP-mmHg), pulmonary capillary wedge pressure (PCWP-ínmHg), cardiac index (CI-L/min/m^2), cardiac output (CO-L/min), systemic vascular resistance (SVR-dyne.s.cm-5), pulmonary vascular resistance (PVR- dyne.s.cm-5), left ventricular stroke work index (LWSVI-g.m/m^2) and stroke volume index (SVI-mL/m^2) were measured. The measured hemodynamic data were monitored in periods of preoperative, during operation, at postoperative 2, 6, 12 hours and postoperative day 1. By using data obtained with Swan-Ganz catheter, LWSVI and SVI were calculated according to following formulas:

LWSVI - SVI.(MAP-PCWP).0.0136 (Normal-43 to 56 g.m/m^2)

SVI = CI/HR (Normal=40±7 rnL/m^2),

SVR and PVR values were calculated by using following formulas:

SVR = MAP-RAP/CO.80, PVR = MPAP-PCWP/CO.80

where MAP=mean arterial pressure, RAP=right atrial pressure, MPAP=mean pulmonary artery pressure, HR=heart rate.

The twelve-lead electrocardiograms of each patient were obtained preoperatively, after CPB, at postoperative 2, 6, 12 hours and postoperative day 1 and 2. Without any interventricular conduction disturbance, all changes of ST segment exceeding 3 mm were suggested as findings of either ischemia or infarction. Moreover, patients were continuously monitored along intensive care period (at least 12 hours) using bedside monitors (Horizon XL, Mennen Medical Inc, Clerence NY) having capability of automatic recall. A11 important changes were noted by monitor nurses.

Serum creatine kinase (CK) and myocardial isoenzyme of creatine kinase (CK-MB) measurements were also made in both groups. The blood samples were drawn preoperatively, at immediate postoperative period, 12th hour and on postoperative day 1 and 2.

Evaluations of Cardiac Arrhhythmia

None of the patients had received prophylactic antiarrhythmic therapy. The VTs detected as either in multifocal origin or leading hypotension, more frequent than 10/min. and R on T phenomenon were treated. In the absence of these criterias such as, couplets, triplets or transient tachyarrhythmias, any intervention was withheld. The teatment was carried on with lidocaine administered in 1 mg/kg dosage as preliminary and followed by infusion up to 3 to 4 mg/min. In such cases that this management had failed or coupled with supraventricular tachyarrhythmias propaphenon HCL was added to therapy as 1 to 2 mg/kg in dosages. In cases whose SVTs unresponsive to ion balancing interventions and progressing to atrial fibrillation, digoxin was commenced with 1.5 mg/24 h in loading dose. There was not any need to use electrical cardioversion.

Table 1. Modified Lown Grades.

Lown Grade	Ventricular Premature Beats	Modified Lown Grades
0	None	None
1A	< 1/min	
IB	> l/min,< 30/h	Occasional
2	>30/h	Frequent
3	Multiformed	Multiformed
4A	Couplets	
4B	Salvo	Repetetive
5	R on T,Ventrikulär tachycardia	Sustained

Ventricular tachyarrhythmias were graded according to Modified Lown Classification (6) (Table 1). Supraventricular arrhythmias were scored and classified as tachyarrhythmia, atrial flutter and atrial fibrillation.

Statistical Analysis

Statistical analysis was performed using the SPSS/PC+ (ver 5.01) computer program. The p values less than 0.05 were considered significant. The comparison of discrete variables and clinical fixed parameters between two groups was performed via X^2 test. The mean and standart error of mean (SEM) values of all parameters were calculated and indicated. "Cochran Q" and "Friedman Two-Way Annova" tests were used to evaluate the significance of change, in clinical discrete variables proportional to sampling time, within a group. The comparison of two groups regarding preoperative fixed variables and nominal baseline characteristics (age, gender, EF, CPB and cross clamping times) was performed via "Mann-Whitney U-Wilcoxon Rank Sum W Test". For comparison of biochemical and hemodynamic variables between two groups, "Student's t" test was performed after the completion of variance analyses with "Levene" test. The significance of changes in biochemical and hemodynamic variables proportional to sampling times within a group was examined with "95 Percent Newman-Keuls Multiple Range and Variance analysis". The mean differences of hemodynamic, biochemical and electrocardiographic variables between both groups and interaction of these differences, with sampling time examined with "Split Plot" variance analysis. "The paired t test" was also used to examine the differences between both groups for each sampling time.

Results

There was not any significant difference in, baseline characteristics (age, gender, medication, cardiac class) and operative data (graft number, pump time) (Table 2). There was not any significant difference between two groups regarding preoperative hemodynamic, rhythm and biochemical parameters. There was not any mortality in both groups. In postoperative period, two patients in magnesium group were underwent lengthened assisted ventilation exceeding 48 hours because of respiratory distress, whereas, 4 patients in control group had undergone lengthened ventilatory support and 1 patient had received intra-aortic ballon pump (IABP) support, not longer than 24 hours. There was not any significant difference in morbidity rates of both groups.

Hemodynamic Effects of Magnesium Prophylaxis

The serum magnesium concentration of study group was significantly higher than those of control group in all sampling times (p=0.001) (Table 4) (Figure 1). The serum magnesium concentration trend of study group also showed a significant increase in comparison of preoperative and later sampling times, whereas, the control group showed a significant reduction in sampling times later than preoperative observations. In conclusion, magnesium levels of control group reduced significantly in postoperative period (p<0.001). Calcium and potassium measurements were also made coinstantly with magnesium and detected deficiencies were replaced immediately. A significant difference was not detected between groups regarding these ion levels.

The mean cardiac index of patients in study group was 2.748±0.73, and of control group was 2.793±0.81 L/min/m^2, being the differences between groups (p=0.673) as well as group-sampling time interactions (p=0.777) were insignificant. The CI values of both groups showed a significantly increasing trend along postoperative observation periods (Table 3).

Table 2. Characteristics of patients in two groups. (NYHA: New York Heart Association, COPD: Chronic obstructive pulmonary disease, MI: Myocardial infarction.)

Operative and demografic data	Magnesium	Control	p Value
Age(years-mean)	57,52 ±9,61	57,96 ± 8,98	0,813
Sex (M/F-number)	47/7 = (86/14)%	40/10 =(80/20)%	0,424
NYHA(I,II,III,IV)	5,35,8,2	4,35,8,3	0,958
Ejection fraction (%)	51,16 ±9,24	47,46 ± 11,21	0,075
Cross-clamp time(min)	57,20 ±28,73	58,92 ± 18,53	0,723
Cardiopulmonary bypass time(min)	89,94 ±33,51	91,70 ±26,64	0,772
Number of gafts	3,28 ± 0,86	3,26 ± 0,78	0,903
Preoperative medications	(+ /-)	(+/-)	
Calcium blockers	23 / 27, (46/54) %	24 / 26, (48/52) %	0.841
P blockers	42 /8, (84/16)%	42/ 8, (84/16)%	1
Diuretics	50/0, (100/0) %	45 /5,(90/10)%	0.056
Digoksin	49/ 1,(98/2)%	45 /5, (90/10)%	0.204
Dysrhythmia and disease history	(+/-)	(+/-)	
Diabetes	42 / 8, (84/16)%	39/ 11, (78/22) %	0.444
Renal insufficiency	50 /0,(100/0)%	50/0,(100/0)%	1
COPD	50 /0,(100/0)%	49/ 1,(98/2)%	1
Prior MI	33 / 17, (66/34) %	25 / 25, (50/50) %	0.105
Supraventricular arrhythmia	50 /0,(100/0)%	49/ 1,(98/2)%	1
Ventricular arrhythmia	45 /5, (90/10) %	50/0, (100/0) %	0.056
Sinus tachycardia	50/0,(100/0)%	50/0,(100/0)%	1

Table 3. Hemodynamic variables of both groups. (CI. Cardiac index, SVR: Systemic vascular resistance, PVR: Pulmonary vascular resistance, SVI: Stroke volume index, LVSWI: Left ventricular stroke work index, Preop: Before the magnesium administration,Perop: End of operation.)

Variable	Mean	Prcop.	Perop.	2 hours	6 hours	12 hours	Day 1
CI (L/min/m^2)							
Magnesium	2.748±0.73	2.076± 0.55	2.736±0,76	2.628 ± 0.85	2.874 ± 0.76	3.154 ±0.74	3.016 ±0.76
Control	2.793±0.81	2.134±0.72	2.646±0.86	2.798 ± 0.90	2.982 ± 0.80	3.158 ±0.79	3.040 ± 0.80
p value	0.673	0.630	0.520	0.307	0.540	0.980	0.886
SVR (dync.s.cm-5)							
Magnesium	1156±372	1563 ± 506	1084 ±383	1194 ±476	1069 ± 489	981 ± 318	1046 ±361
Control	1178±403	1485 ± 650	1216 ±618	1240± 586	1056± 366	1025± 323	1046 ±330
p value	0.699	0.328	0.231	0.660	0.890	0.560	0.990
PVR (dyne.s.cm-5)							
Magnesium	167.7±67	150.6±71	147.2 ± 66	177.1 ±64	177.4 ± 70	166.5 ± 61	187.5 ±69
Control	172.4±80	154.6 ± 80	164.3 ± 95	190.7 ±96	166.7 ±69	179.1 ±65	179 ±71
p value	0.618	0.789	0.215	0.380	0.470	0.382	0.472
SVI (ml/m^2))							
Magnesium	28.46±7.88	24.99± 7.17	29.1 ±9.75	25.75 ±9.98	29.53 ± 10	30.60± 6.53	30.79± 6.98
Control	27.32±8.33	22.33± 7.30	26.28±10.2	25.97 ±8.37	28.64 ± 7.69	29.60 ± 7.73	30.59 ± 8.84
p value	0.343	0.108	0.128	0.899	0.607	0.541	0.906
LVSWI (g.m/m^2)							
Magnesium	27.60±7.64	25.02± 9.34	26.24±8.78	26.42±10.09	27.79 ± 7.02	29.23± 7.37	30.91 ± 8.28
Control	26.24±8.12	22.27± 7.66	23.79±9.16	25.97± 8.84	27.62± 8.68	28.25± 8.60	29.54 ± 9.80
p value	0.260	0.110	0.150	0.799	0.907	0.796	0.472

Table 4. Alterations in biochemical variables of patients. (CK: Creatine kinase, CK-MB: Myocardial isoenzyme of creatine kinase, Preop: Before tha magnesium administration, Perop: End of operation.)

Variable	Mean	Preop.	Perop.	2 hours	6 hours	12 hours	Day 1	Day 2
Magnesium level (mEq/L)								
Magnesium	2.037±0.51	1.813± 0.32	2.313±0.68	2.117±0.49	2.033±0.54	2.107±0.50	2.104±0.49	1.775 ± 0.43
Control	1.738±0.37	1,891 ±0.29	2.025±0.46	1.808±O.5O	1.625±0.48	1.717±0.40	1.537± 0.39	1,.552±0.31
p value	0.001	0.09	0.005	0.0006	6.03.10-6	1.39.10-6	1.48.10-6	0.00013
CK (IU/L)			Perop.		12 hours			
Magnesium	465±184	73.8±52.96	337.9±193.1		477.7±239.4		678.4±578.7	758±897
Control	466±221	88± 114.4	323Ü74.4		490±252.8		684±519	745±644
p value	0.990	0.439	0.680		0.796		0.958	0.976
CK-MB (IU/L)								
Magnesium	33.94±20.8	17.72±7.4	55.86±24.47		34.02il2.07		32.34±15.26	29.76±21.73
Control	39.27±25.6	1 Ç 1 R*£ ^7	55.56*25.86		45.98±25.80		44.58±41.25	35.06±30.55
p value	0.068	0.079	0.953		0.002		0.043	0.278

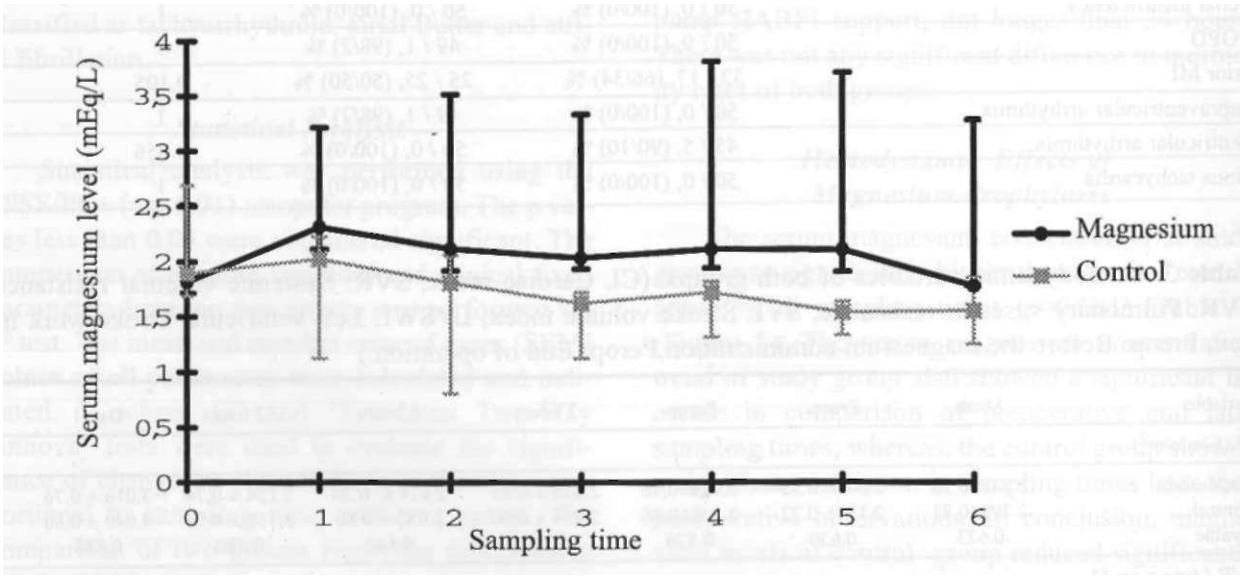

Figure 1. Alterations in serum magnesium levels of patients according to sampling times. (Sampling time 0: Preoperative, 1: Perioperative-end of operation, 2: Postoperative 2nd hour, 3: Postoperative 6th hour, 4: Postoperative 12th hour, 5: Postoperative day one, 6: Postoperative day two.)

There was not any significant difference in comparison of SVR measurements, as both between two groups (p=0.699) and group-time interaction (p=0.538). Mean SVR values of study and control groups were 1156±372 and 1178±478 mmHg, respectively. In both groups, the postoperative SVR values had become significantly less than the preoperative ones (p<0.05) (Table 3).

Mean PVR values of study and control groups were 167.7±67 and 172.4±80 mmHg, respectively and the difference was not significant between two groups (p=0.618) as well as group-time interaction (p=0.485). The PVR values of both groups routed on a trend similar to that of SVR values, during postoperative period (Table 3).

Mean values of SVI calculations in study and control groups were 28.46±7.88 and 27.32±8.33 mL/m2 respectively and yielded no significant difference in both between two groups (p=0.343) and group-time interaction (p=0.571). The mean

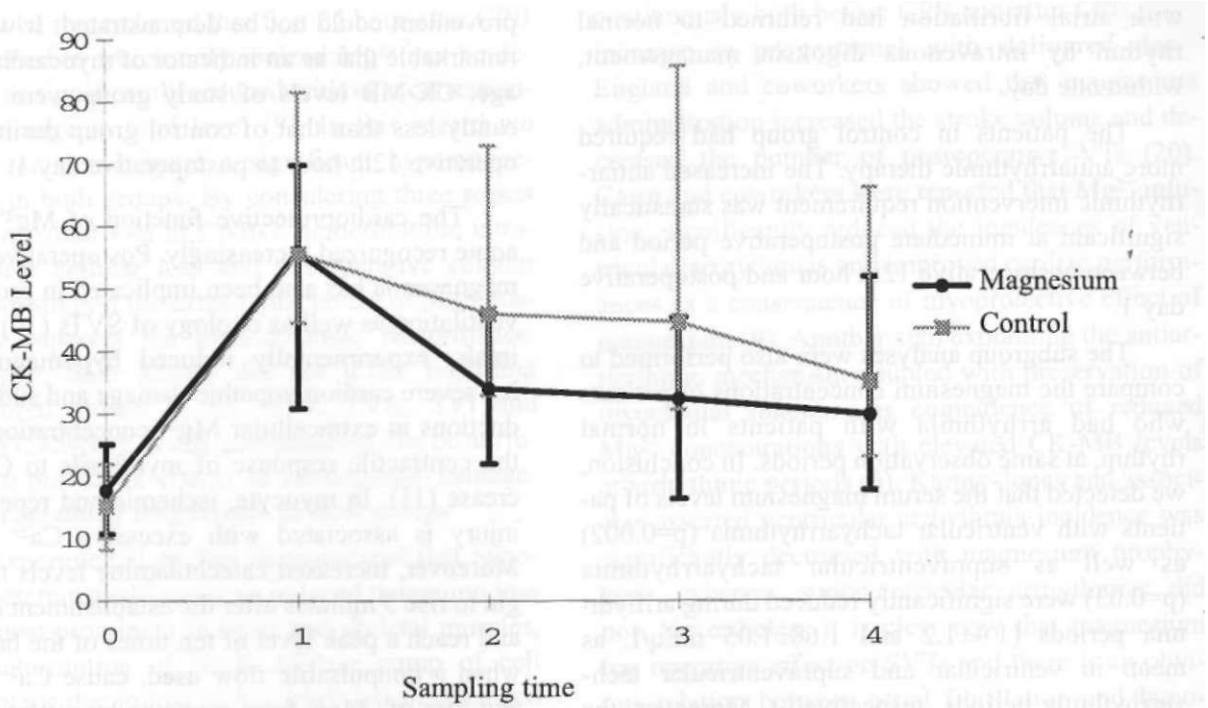

Figure 2. Alterations in myocardial isoenzyme of creatine kinase (CK-MB) levels of patients according to sampling times. (Sampling time 0: Preoperative, 1: Peroperative-end of operation, 2: Postoperative 12th hour, 3: Postoperative day one, 4: Postoperative day two.)

LVSWI values of study and control groups were 27.60±8.76 and 26.24±8.38 g.m/m2, respectively and showed no significant difference similarly to SVI values, as both between groups (p=0.260) and group-time interaction (p=0.711) (Table 3).

As a biochemical parameter, CK evaluations showed no significant difference before and after operation (p=0.990), as well as between two groups along the course of study (p=0.998). Although the mean values of myocardial isoenzyme of creatine kinase (CK-MB) examinations before and after operation were similar in both groups and showed no significant difference, CK-MB levels of study group were significantly less than those of control group at postoperative 12th hour (p=0.002) and postoperative day 1 measurements (p=0.043) (Table 4) (Figure 2). The CK-MB levels in both groups coursed in a similar trend and showed a stable decline after the peroperative measurements.

The electrocardiographic ST segment analyses of both groups showed no significant difference along the course of study (p=0.363 for study and p=0.215 for control group). There was not any significant difference also, regarding postoperative inotropic or IABP support requirement of each group (p=0.298 and p=0.416 for study and control group respectively).

Cardiac Rhythm and Dysrhythmia Evaluations

Ventricular tachyarrhythmias were evaluated according to Modified Lown Grades. Despite the numerical proponderance as well as higher grades of ventricular arrhythmias in control group (28% - 14 patients versus 12% - 6 patients), differences did not reach a significant level (p=0.063). It must be considered that none of the patients in both groups had undergone ventricular tachycardia or fibrillation, indicated as Lown grade 5.

The atrial tachyarrhytmias were graded as atrial arrhythmias or premature beats fewer than 20/min, atrial flutter and atrial fibrillation. We detected that atrial tachyarrhythmia incidence of study group significantly less than that of control group along the course of study. If only atrial fibrillation incidence was considered, despite the numerical abundance in control group (3 versus no patient in study group), the difference did not reach a significant level (p=0.950). Each of 3 patients

with atrial fibrillation had returned to normal rhythm by intravenous digoksin management, within one day.

The patients in control group had required more antiarrhythmic therapy. The increased antiarrhythmic intervention requirement was statistically significant at immediate postoperative period and between postoperative 12th hour and postoperative day 1.

The subgroup analyses were also performed to compare the magnesium concentrations of patients who had arrhythmia with patients in normal rhythm, at same observation periods. In conclusion, wc detected that the serum magnesium levels of patients with ventricular tachyaiThythmia (p=0.002) as well as supraventricular tachyarrhythmia (p=0.03) were significantly reduced during arrhythmia periods (1.4±1.2 and 1.68Ü.05 mEq/L as mean in ventricular and supraventricular tachyanfiytlimia periods, respectively). Moreover, the CK-MB levels of patients in supraventricular arrhythmia periods were significantly elevated (p<0.05). Randomized comparisons did not yield a significant result.

Discussion

Most of the an-hythmias in CABG can be managed with medical therapy or electrical cardioversion. However, lots of these interventions have some untoward effects, such as to depress myocardial contractility due to inherent P blocker capacity or to increase myocardial oxygen demand. The alterations in concentrations of some ions like potassium and magnesium play a major role in etiology of postoperative arrhytlimias. In this respect, it is asserted that the correction of the deficiencies of Mg^{2+} enable to prevent arrhythmias and protect normal sinus rhythm. This study demonstrated that the replacement of Mg^{2+} in a total 10.5 g (85 mEq) dose by delivering 1.5 g(12.16 mEq) magnesium sulfate in seven consecutive doses during postoperative 24 hours, to patients undergoing CABG remarkably reduced the postoperative supraventricular tachyarrhythmia (SVTs) incidence and antiarrhythmic therapy requirement in study group having significantly elevated Mg^{2+} level. The antiarrhythmic potential of Mg^{2+} on ventricular tachyarrhytmias (VTs) as well as in myocardial improvement could not be demonstrated. It was also remarkable that as an indicator of myocardial damage, CK-MB levels of study group were significantly less than that of control group during postoperative 12th hour to postoperative day 1.

The cardioprotective function of Mg^{2+} is become recognized increasingly. Postoperative hypomagnesemia has also been implicated in prolonged ventilation as well as etiology of SVTs (10). In animals, experimentally induced hypomagnesemia led severe cardiomyopathy damage and sudden reductions in extracellular Mg^{2+} concentration made the contractile response of myofibrils to Ca^{2+} increase (11). In myocyte, ischemia and reperfusion injury is associated with excessive Ca^{2+} influx. Moreover, increased catecholamine levels that begin to rise 5 minutes after the establishment of CPB and reach a peak level of ten times of the baseline, when a nonpulsatile flow used, cause Ca^{2+} influx and loss of Mg^{2+} from myocyte by cyclic adenosine monophosphate mediated (3 receptor stimulation. Excessive Ca^{2+} load subsequently causes an increase in diastolic tone (12). Data from animal studies suggest, Mg^{2+} has a direct Ca^{2+} antagonistic effect on vascular smooth muscle cell (13). Kimura and colleagues showed that Mg^{2+} inhibits the periodic as well as the tonic contractions of isolated human coronary arteries more efficiently than diltiazem and nitroglycerin (14). Data from the second Leichester Intravenous Magnesium Intervention Trial (LIMIT-2) demonstrated a 24% reduction in mortality and a 25% reduction in the incidence of heart failure as a consequence of reduction in infarct size (15). Brookes and Fry reported that almost 24 hours after a cardiac operation the ionized Mg^{2+} is significantly reduced without any change in total level due to a Mg^{2+} binding ligand in unknown origin (16). Besides transcellular changes, surgical stress and ischemia induced catecholamine release and subsequent lypolysis causes the binding of Mg^{2+} by free fatty acids. Lareau and colleagues observed that isolated human atrial trabecular tissues in a Mg^{2+} rich solution had better contractile power and had more adenilate reserves than ones in Mg^{2+} poor solution (17).

Caspi and coworkers reported that magnesium sulfate infusions in postoperative period significantly improved the hemodynamic performances.

It must be remembered that first 24 hour after CPB is a period in which only ionized Mg^{2+} can be detected as significantly reduced without a corresponding change in total level (9). In this regard we could not demonstrate a significant hypomagnesemia in both groups. By considering three routes of magnesium loss in CABG; hemodilution, intraoperative cellular loss and postoperative cellular loss, we suggest the extra-replacement of Mg^{2+} positively supports the hemodynamic performance. Although, both groups did not differ regarding monitored values of CI, SVR, PVR, SVI and LVSWI, absence of any complication can be attributed to protective effects of cardioplegic management containing magnesium in both groups.

Experimental studies demonstrated that hypomagnesemia could cause an induced potassium loss that most prominent in heart and skeletal muscles, and interruption of Na-K ATPase pump of cell membrane due to loss of free Mg^{2+} led an enhanced loss of potassium from cell. Furthermore, it was asserted that the replacement of potassium was more difficult in hypomagnesemia that had a 42% coincidence rate with hypocalemia (18). The antiarrhythmic properties of magnesium on VTs probably related to its ameliorating effects on hypocalemia (9). We could not detect a corresponding change between potassium and magnesium, along the course of study. The additional replacements of potassium and calcium to alleviate any arrhythmogenic property of deficiency of these ions could be implicated in this result as well as in indifferent VTs incidences of both groups.

Magnesium is a cofactor of some enzymes such as, Na-K ATPase and Ca ATPase that effects membrane stabilization. If extracellular Mg^{2+} concentration rises two folds of baseline, an additional 6 mV energy is required to depolarize the membrane. It makes the sensitive period shorten, and decreases the reentry formation as well as elevates ventricular fibrillation threshold. Magnesium also diminishes dysrhythmias in ischemic origin. Rasmussen reported that arrhythmia incidence of magnesium group was significantly less than that of placebo group (21% versus 42%) (19). The antiarrhythmic potential of magnesium is more prominent when delivered after CPB rather than before CPB and it increases further if delivered continuously both before CPB and after CPB. This increase is proportional with delivered dose. England and coworkers showed that magnesium administration increased the stroke volume and decreased the number of postoperative VTs (20). Caspi and coworkers were reported that Mg^{2+} infusion, significantly reduced the incidences of ventricular arrhythmias and improved cardiac performances as a consequence of myoprotective effect of magnesium (9). Another sign explaining the antiarrhythmic mechanism coupled with preservation of myocardial functions is coincidence of reduced Mg^{2+} concentrations with elevated CK-MB levels at arrhythmic periods (6). Karmy-Jones and associates asserted ventricular arrhythmia incidence was significantly decreased with magnesium prophylaxis, whereas supraventricular arrhythmias did not. Nevertheless it is clear now that magnesium has operative effect on SVTs and there is an obvious relation between atrial fibrillation and hypomagnesemia (6, 13).

We did not observe any significant benefit of magnesium prophylaxis on VTs, whereas there was a significant decrease in SVTs incidence. Moreover, antiarrhythmic intervention incidence was also significantly less in magnesium group. Although ventricular arrhythmia incidence did not differ significantly, there were 8 patients in control group with VTs in modified Lown grade 2 or 3, whereas there were only 2 patients in magnesium group in corresponding grades. There was not also significant difference between two groups regarding cardiac performances in arrhythmia periods ($p>0.05$). The most obvious sign of antiarrhythmic property of Mg^{2+} was the detection of significantly reduced Mg^{2+} levels in both SVTs and VTs periods. However, Karmy-Jones group did not reported a significant fall of Mg^{2+} level in SVTs periods (6). We suggest that myocardial protective effect of magnesium is basic factor underlying its antiarrhythmic properties. Since the potassium deficits of patients were replaced immediately along the study, it is not possible to say potassium regulating effects of magnesium play an important role. The more perfect results can be obtained via analysis of delayed evoked potentials instead of simple electrocardiographic evaluations.

Although the cardiac performance tests did not yield significant results regarding cardioprotective function of magnesium, the CK-MB levels were detected as significantly elevated at measurements of postoperative 12th hour to postoperative day 1. in which times the most of arrhythmias either ventricular or supraventricular had occurred. This is a considerable result indicating cardioprotective function of magnesium.

The results of our study suggest that magnesium prophylaxis has ability to reduce supraventricular and somewhat ventricular arrhythmias occurred after coronary artery bypass grafting, without any complicating effect on cardiac or respiratory functions. The antiarrhythmic property of magnesium can be attributed to improved myocardial protection after ischemic arrest.

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